Ortho-phthalaldehyde

[§81-3] Acute Inhalation Study/Rat

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DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat; OPPTS 870.1300, [§81-3]

DP BARCODE: D285992

SUBMISSION CODE: S622751

P.C. CODE: 129017

TEST MATERIAL (PURITY): Ortho-phthalaldehyde (99.6% a.i.)

SYNONYMS: 1,2-Benzenedicarboxaldehyde, Ucarcide™ P200 Antimicrobial

CITATION: Hoffman, Gary M. (2002). Ortho-Phthalaldehyde: An Acute (4-Hour) Inhalation Toxicity Study in the Rat Via Whole-Body Exposure. Huntingdon Life Sciences. Study Number 98-5348, June 29, 1998. MRID No. 45702501. Unpublished.

SPONSOR: Union Carbide Corporation, Danbury, CT

EXECUTIVE SUMMARY:

In an acute inhalation toxicity study (MRID 457025-01), a single group of 5 male and 5 female young adult Sprague-Dawley CD® rats was exposed via inhalation to Ortho-phthalaldehyde (99.6% a.i.) for four hours via a single whole-body exposure at a nominal concentration of 0.90 mg/L (near-saturated vapor). Animals then were observed for 14 days. There were no significant treatment-related clinical signs, necropsy findings, or changes in body weight.

In this study, the inhalation LC_{50} for male and female albino rats was determined to be greater than 0.90 mg/L.

This acute inhalation toxicity study is classified as **Not-Acceptable** (but upgradable). The actual concentration of the test material in the breathing zone was not determined. Without this information, there is no way to accurately assess exposure. Therefore, this study does not satisfy the guideline requirements for an acute inhalation toxicity study (OPPTS 870.1300) in rodents. The study can be upgraded by measuring the concentration of the test material.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Data Confidentiality and Quality Assurance

statements were included in the report. The GLP statement, which was signed by the Sponsor, indicated that the study was not conducted in accordance with EPA GLP Standards (40 CFR Part 160), but rather was conducted in accordance with Organization for Economic Cooperation and Development (OECD) GLP Principles (OECD, 1998a). A separate Compliance Statement signed by the Study Director, however, indicated that the study was not conducted in accordance with OECD Principles of GLP ENV/MC/CHEM/(98)17 because: (1) the testing facility lacked knowledge of procedures used for feed and water analyses, and (2) GLP Chemical Characterization of the test material was not conducted by the Sponsor. The Study Director indicated, however, that these deviations were not considered to affect the interpretation or results of the study.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material: Ortho-phthalaldehyde

   Description: Faintly yellow solid

   Lot/Batch #: GISHER-805

   Purity: 99.6% active ingredient

   CAS #: 643-79-8

   Storage Conditions: In the dark at room temperature

   Characterization of Compound: No information provided; study authors noted that identity, strength, purity, homogeneity, composition, and stability of the test material were the responsibility of the Sponsor.

2. Vehicle and/or Positive Control: The test material was used as received.

3. Test Animals: Albino rat (outbred) VAF/Plus®

   Strain: Sprague-Dawley derived (CD®) [Crl: CD®(SD)BR]

   Age at Dosing: Approximately 10 weeks

   Weight at Dosing: The mean body weight of male animals prior to exposure was 329 grams (range 320-356 grams). The mean body weight of female animals prior to exposure was 225 grams (range 219-233 grams). Weight variation in the animals did not exceed ±20 percent of the mean weight.

   Source: Charles River Laboratories, Kingston, New York

   Diet: Animals were provided with certified Rodent Diet, #5002, in pellet form during acclimation and in mash form thereafter, *ad libitum*. Food was withheld during exposure. Analysis of feed was performed by PMI Nutrition International; the study report indicated that results are available from the testing facility.

Water: Animals were provided with water *ad libitum* from an automated watering system. Water was withheld during exposure. Analysis of water was performed by Elizabethtown Water Company; the study report indicated that monthly water analyses are available from the testing facility. Biannual chemical and microbiological analyses of water samples collected by the facility also are available.

Housing: During the acclimation period, animals were housed in groups in suspended, stainless steel, wire mesh cages. During all other periods, animals were housed individually.

Environmental conditions:

Temperature: 20-24° C (prior to and following exposure); 20-23° C (during exposure)

Humidity: 53-88 percent (prior to and following exposure); 43-68 percent (during exposure)

Photo period: 12 hours light/12 hours dark cycle

Acclimation Period: 14 days

B. STUDY DESIGN AND METHODS

1. In Life Dates

Start: August 4, 1998 (initiation of exposure)

End: August 18, 1998 (terminal sacrifice)

2. Exposure Conditions

Animals were exposed whole-body in 100 Liter Plexiglas® and glass exposure chambers. An appropriate amount of pure oxygen was added to the chamber as needed to maintain the oxygen level between 19 and 21 percent during exposure. Total chamber flow, static pressure, temperature, humidity, and oxygen level were recorded once at the initiation of exposure and approximately every half hour during exposure. Chamber temperature and relative humidity were recorded approximately every half hour during exposure and maintained within 20-23° C and 43-68 percent, respectively.

Figure 1 and Appendix A of the study report describe the equipment details. The whole-body chamber was divided into an upper and lower section by a horizontal Plexiglas® divider. The test material was placed in a stainless steel bowl in the upper section of the sealed chamber and the contents were allowed to equilibrate overnight. A fan circulated the air for one minute at fifteen-minute intervals prior to exposure and operated continuously during the exposure period to

maintain equilibrium. For the exposure, animals were placed in the lower section of the chamber. Removal of the section divider initiated exposure to the vapor.

3. Animal Assignment and Treatment

A single group of five males and five females was exposed to the test material for four hours via whole-body inhalation with the test article provided as a vapor. The study report indicated that animals were selected from an in-house population. The study report did not indicate, however, that a randomization procedure was used to assign the animals to the test group.

During the exposure period, animals were observed as a group for signs of toxicity at 15-minute intervals during the first hour and then hourly for the remainder of the 4-hour exposure. Animals were observed individually for signs of toxicity immediately upon removal from the chamber and hourly for two hours on the day of exposure (Day 1). They were observed once daily for 14 days after the day of dosing (Days 2 through 15). Animals were weighed on the following days: Day 1 (just prior to dosing), Day 8, and Day 15 (just prior to sacrifice and necropsy). As indicated, sacrifice and necropsy of survivors occurred on day 15.

4. Chamber Concentration

The specific time for the test article vapor to reach equilibrium was not provided. The study report indicated that the test material was allowed to equilibrate in the chamber overnight.

The nominal concentration was determined by weighing the stainless steel bowl containing the test material before and after exposure, dividing the difference in these weights by the total volume of the exposure chamber (1000 Liters), and multiplying the dividend by 1000 mg/g. The nominal exposure concentration was determined to be 0.90 mg of test material per liter of air, which was considered to be a near-saturated vapor atmosphere.

5. Statistics

No statistical evaluations were performed in this study.

II. RESULTS AND DISCUSSION

A. MORTALITY

No deaths occurred during the exposure or the 14-day post-exposure period. Table 4 of the study report summarizes the mortality results for the individual animals.

B. CLINICAL OBSERVATIONS

The study report indicates that individual examinations included observations of general

condition, skin, fur, eyes, nose, oral cavity, abdomen, and external genitalia, and evaluations of respiration and palpation for tissue masses. Red nasal discharge was observed in two male animals sporadically during the 14-day post-exposure observation period. The study report indicates that this discharge was not considered treatment-related. No signs were observed, however, during exposure or during the 2-hour post-exposure observation period. No other remarkable effects were observed.

C. BODY WEIGHT

Slight body weight losses (one gram each) were observed for two female rats from Day 8 to Day 15. All other animals gained weight during the 14-day observation period, and no other remarkable body weight changes were observed.

D. NECROPSY

Complete macroscopic postmortem examinations were performed on all animals. No abnormalities were observed at the terminal necropsy for all examined tissues in all animals. Table 4 of the study report summarizes the necropsy observations.

E. DEFICIENCIES

The study report contains one major deficiency when compared to EPA's guideline requirements for an acute inhalation toxicity study (OPPTS 870.1300) in rodents. The actual concentration of the test material in the breathing zone was not determined. Without this information, there is no way to accurately assess exposure. The guideline requirements indicate that the actual concentrations of the test material should be measured in the breathing zone. Multiple measurements of the chamber concentration should be taken during the exposure period in order to demonstrate that the actual concentration of the test material is held constant and monitored continuously or intermittently.

The study authors evaluated 0.90 mg/L of test material because this concentration was considered to be a near-saturated vapor atmosphere. OPPTS 870.1300 guidelines recommend an exposure concentration of 2 mg/L for four hours, or the maximum attainable concentration where this is not possible due to physical or chemical properties of the test material. The study report did not describe the physical properties of the test material, but rather indicated that the physical properties of the test material are the responsibility of the sponsor. Obtaining information regarding the selection of the lower concentration is recommended. This is a minor deficiency that does not affect the outcome of the study.

The study report did not indicate that a randomization system was used to assign the animals to the test group. OPPTS 870.1300 guidelines require a system to randomly

assign animals to the test group. Obtaining information to determine if a randomization system was used for assignment of animals to the test group is recommended. This is a minor deficiency that does not affect the outcome of the study.